REMARKS

The Office Action issued by the Examiner and the citations referred to in the office action have been carefully considered. Reconsideration is respectfully requested.

By this amendment minor issues in the clams have been rectified which could have given concern under Section 112, paragraph 2.

Also the claims 1, 10 and 25 have been amended to focus on the feature of thyroid disease and hence the claims now additionally claim:

> analysis of the total T4, total T3, free T4, free T3, T3 autoantibody, T4 autoantibody and thyroglobulin autoantibody;
>
> establishing for thyroid disease analysis optimal levels, the levels being defined by a range different to a laboratory reference range as presented in the laboratory report, there being at least one category of the adequate optimal levels, therapeutic response optimal levels, the minimal expectations optimal levels; or the optimal levels for confirming autoimmune thyroiditis;
>
> assessing thyroid function as part of the preliminary analysis by determining the correct category, and an analysis based on the laboratory report as applied in the correct category to thereby obtain a supplemental report.

New dependent claims 46 – 48 are added and require:

> applying for the assessment of thyroid function for adult optimal levels the criteria of FT3 is less than 8 pg/mL and FT4 is less than 3 ng/dL.

New dependent claim 49 is dependent on Claim 25 and requires:

> establishing for thyroid disease analysis more than one category of the optimal adequate levels, optimal therapeutic response levels, the optimal minimal expectation levels; or the levels for autoimmune thyroiditis.

In Claim 25 as amended any reference to the icon based system has been deleted. Claims 42 and 45 have been cancelled.

The claims as now submitted are respectfully are patentable over the new art cited by the Examiner. Nowhere, does this art show optimal levels for the different criteria of optimal levels as set out in claims 1, 10 and 25. These features are described in Figures 14A and 15A. In Figure 14A, five lines from the bottom there is described the optimal therapeutic response levels. In Figure 15A, three lines from the top the adequate levels are set out: in Figure 15A, line 8 there are the levels for minimal expectations, and in Figure 15A, six lines from the bottom, there are the levels for autoimmune thyroiditis.

The laboratory reference range is shown in Figures 10 and 14A in the body of the laboratory report, and an exemplary optimal range for adults is shown in Figures 14A and 15A.

More specifically, different numerical levels are specified in the dependent claims. These levels are disclosed in Figure 15A.

These levels are not arbitrary or random. Much experiment has validated the relevance of this range for determining and diagnosing thyroid disease.

The Section 103 rejection of the prior pending clams was premised on a combination of multiple newly applied references. None of the references remotely teaches, discloses or suggests the invention as claims, particularly as now set out in the amended claims.

Specifically Dodds (WO/2001/028415) does not have icons where

> the characteristics of the …icons …[are] such as to be representative of the textual content of the supplementary report, and different selectable icons ….[are] individually related to animal characteristics of age and animal grouping, and …...icons for animal characteristics dependant on age and on animal grouping, and …..icons for groupings of the selected animal groups of adult, puppy-adolescent, geriatric, or large breed dog and …...icons for a disease state, being thyroid disease, the ….icons

being representative of being normal relative to thyroid disease, or abnormal relative to thyroid disease;

Dodds (Dog World 1992) does not disclose anything to do with optimal conditions or ranges.

Filteau (US 2002/0188896) is not related to animal conditions and has nothing to do with thyroid disease.

Hare (Preventive Veterinary Medicine is nothing more than a disclosure of electronically collecting and reporting.

Specifically the Examiner has seemed further to add further references in his argument. None of this makes any sense. The Examiner refers to **Domanik** and **Bean** and yet they are not even cited or applied. What are they? This exhibits the Examiner's lack of relevant references and the stretch to twist references to attempt to meet the claims as submitted. This is not the test of patentability. Obviousness cannot be proven by following the road map of the present inventor.

In addition to all the other features previously described as the basis for patentability, this further characteristic clearly places the invention beyond anything the Examiner could appropriately combine. There is absolutely no teaching of this critical range in any prior art.

Tithe Applicant submits that Examiner inappropriately sought to combine the teaching of the applied art, based on the road map set out by the Applicant in the present claims. This is contrary to the appropriate legal standards. Now, even more so, this further amendment places the patentable subject matter beyond the reach of any of the prior art.

A prior declaration from the inventor Dodds (of US 6,287,254) and the present application states diametrically opposite to the Examiner's unsupported conclusion. Exhibit A to that prior response as previously submitted is not merely a random opinion, but the statement of one of the leading experts in the world in thyroid disease in animals. Such a declaration cannot be casually dismissed by the Examiner as "mere opinion". In fact to the contrary, a person with

actual knowledge of the field on a day to day basis would be the correct expert person. This statement on patentability is convincing as opposed to academic or hypothetical conclusions to the contrary.

The qualifications of such a person, albeit the inventor, Dodds, is that it would not be a disclosure, teaching or suggestion of the present invention, and nor would it have been obvious to modify the teachings of Dodds or to be obvious to try from her knowledge at the time to obtain the features of the present invention, namely the function of generated icons (claims 1 and 10, not claim 25) from her knowledge at the time the present invention was made.

A further Declaration is submitted by the Applicant, Dodds and addresses more specifically the inventiveness of the optimal levels as now claimed.

In view of the above, it is submitted that the claims as presented are patentable over the cited art.

REJECTION UNDER 35 U.S.C. § 103(A)

Although the teaching, suggestion, motivation test is still recognized under *KSR*, --- U.S. ----, 127 S.Ct. 1727, 1742, 167 L.Ed.2d 705 (2007).the test is largely subsumed by the more general principles laid out in *KSR*. Indeed, in any given application, the combination of elements "must do more than yield a predictable result." *Id.* at 1740. Nevertheless, combining elements "in an unexpected and fruitful manner" is sufficient to render an invention non-obvious. *Id.*

More importantly, "a patent composed of several elements **is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art**." KSR *Id.* (emphasis added).

In *KSR*, the Supreme Court addressed such logic in obviousness-type rejections. Importantly, *KSR* specifically forbids obviousness rejections simply because each element was independently known in the prior art. The art cited against the instant application falls into this rubric because they are nothing more than a string of unrelated references showing each of the

claimed elements with tenuous logic to support their combination. The Examiner has failed in his burden to explain any compelling reason why a person of ordinary skill would have combined these references.

No Reasonable Expectation of Success Can Be Inferred from the Combination of References Asserted by the Examiner

a. Reasonable Expectation Standard Reaffirmed Post-*KSR*

The Federal Circuit stated "obviousness does not require absolute predictability of success . . . [a]ll that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-04; 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988). Thus, if a reasonable expectation of success is derived from a reference or combination of references, an invention may be rendered obvious. Conversely, where no reasonable expectation of success is derived, an obviousness rejection is improper. *Id.*

More specifically, *O'Farrell* provides general guidance as to when an invention falls under the reasonable expectation of success rubric, which was subsequently reaffirmed by the Federal Circuit post-*KSR* in *Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1364; 83 U.S.P.Q.2d 1289 (Fed. Cir. 2007). According to the Federal Circuit, "an invention would not be invalid for obviousness if the inventor would have been motivated 'to **vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result**, where the **prior art gave** either **no indication** of which parameters were critical or **no direction** as to which of many possible choices is likely to be successful.'" *Id.* at 1364, *quoting Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165, 77 U.S.P.Q.2d 1865 (Fed. Cir. 2006) (emphasis added).

In a secondary test posited by the Federal Circuit in *Pharmastem*, the court stated "[l]ikewise, an invention would **not be deemed obvious** if **all that was suggested** 'was to **explore a new technology or general approach** that seemed to be a **promising field of experimentation**, where the **prior art gave only general guidance** as to the particular form of

the claimed invention or how to achieve it.'" *Id.*, *quoting Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165, 77 U.S.P.Q.2d 1865 (Fed. Cir. 2006) (emphasis added).

b. No Reasonable Expectation of Success Where Numerous Possible Choices or Requirement to Vary All The Parameters

Using the first of the standards promulgated by the Federal Circuit, the combination of references cited by the Examiner against the claims have no reasonable expectation of success because the prior art references give no indication of critical parameters or direction as to how to achieve the claimed invention. Using any one of the prior art as the starting point to arrive at the claimed references cited against the instant application would require numerous choices in direction and experimentation, as well as variance of many parameters to arrive at the claimed invention.

For the reasons stated above, the prior art references cited against the claims also fail the second standard promulgated by the Federal Circuit. An invention is not obvious if all that was suggested is to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. *Pharmastem* at 1364. In other words, the combination of references must give specific guidance to arrive at the claimed invention.

More specifically, the prior art references cited against the instant claims include references directed to different fields. These prior art references alone do not even provide even general guidance to the instant problem and claimed solution.

In fact, the combination of these references makes sense **only** when viewed in the context of the specification and claims. Alone, they don't get a person of ordinary skill in the art any closer to an expectation of success because they simply don't have any guidance, even when combined, to guide a person of ordinary skill in the art to the claimed result without significant detective work.

Recently the Federal Circuit reaffirmed the obviousness standard in *Ortho-McNeil Pharmaceutical, Inc., v. Mylan Laboratories* as 520 F.3d 1358 at 1364 to 1365; 86 U.S.P.Q. 2d 1196 (Fed. Cir. 2008). The standard is quoted as follows:

> Mylan cites *KSR International Co. v. Teleflex Inc.*, for the proposition that "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." --- U.S. ----, 127 S.Ct. 1727, 1742, 167 L.Ed.2d 705 (2007). The record, however, shows that even if an ordinarily skilled artisan sought an FBPase inhibitor, that person would not have chosen topiramate. Moreover this invention, contrary to Mylan's characterization, does not present a finite (and small in the context of the art) number of options easily traversed to show obviousness. The passage above in *KSR* posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness. In this case, the record shows that a person of ordinary skill would not even be likely to start with 2,3:4,5 di-isopropylidene fructose (DPF), as Dr. Maryanoff did. Beyond that step, however, the ordinarily skilled artisan would have to have some reason to select (among several unpredictable alternatives) the exact route that produced topiramate as an intermediate. Even beyond that, the ordinary artisan in this field would have had to (at the time of invention without any clue of potential utility of topiramate) stop at that intermediate and test it for properties far afield from the purpose for the development in the first place (epilepsy rather than diabetes). In sum, this clearly is not the easily traversed, small and finite number of alternatives that *KSR* suggested might support an inference of obviousness. *Id.* at 1742.
>
> In other words, Mylan's expert, Dr. Anderson, simply retraced the path of the inventor with hindsight, discounted the number and complexity of the alternatives, and concluded that the invention of topiramate was obvious. Of course, this reasoning is always inappropriate for an obviousness test based on the language of Title 35 that requires the analysis to examine "the subject matter as a whole" to ascertain if it "would have been obvious at the time the invention was made." 35 U.S.C. § 103(a) (emphasis in original). In retrospect, Dr. Maryanoff's pathway to the invention, of course, seems to follow the logical steps to produce these properties, but at

the time of invention, the inventor's insights, willingness to confront and overcome obstacles, and yes, even serendipity, cannot be discounted.

As this court has explained, however, a flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis such as occurred in this case. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed.Cir.2007) ("[A]s the Supreme Court suggests, a flexible approach to the TSM test prevents hindsight and focuses on evidence before the time of invention."). The TSM test, flexibly applied, merely assures that the obviousness test proceeds on the basis of evidence-teachings, suggestions (a tellingly broad term), or motivations (an equally broad term)-that arise before the time of invention as the statute requires. As *KSR* requires, those teachings, suggestions, or motivations need not always be written references but may be found within the knowledge and creativity of ordinarily skilled artisans.

In this case, the record amply supports the district court's finding of nonobviousness. This court detects no rigid application of the evidentiary requirements for obviousness in the district court's analysis. As noted above, the challenges of this inventive process would have prevented one of ordinary skill in this art from traversing the multiple obstacles to easily produce the invention in light of the evidence available at the time of invention. Of particular importance beyond the prima facie analysis, this court also detects evidence of objective criteria showing nonobviousness. Specifically, the record shows powerful unexpected results (anticonvulsive activity) for topiramate. The record also shows skepticism of experts and copying-other respected sources of objective evidence of nonobviousness-as well as commercial success. As this court has repeatedly explained, this evidence is not just a cumulative or confirmatory part of the obviousness calculus but constitutes independent evidence of nonobviousness. *Catalina Lighting, Inc. v. Lamps Plus, Inc.*, 295 F.3d 1277, 1288 (Fed.Cir.2002) ("Objective indicia may often be the most probative and cogent evidence of nonobviousness in the record.") (internal citation omitted). *See also PharmaStem Therapeutics Inc. v. Viacell, Inc.*, 491 F.3d 1342; *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369.

The KSR Guidelines as applied to the instant application support inventiveness since the inventor has discovered and claimed the optimal ranges as opposed to the general conditions. In analyzing these improved results, one is struck by the difference in kind attributable to invented range, and logically the improvements could not flow equally well from changes in degree resulting from routine variation or experiment of the general conditions.

Further there is commercial success arising from the invented features to support patentability.

There was an almost limitless array of variables, and the correct thyroid diagnosis characteristics and ranges for adult optimal levels the criteria of FT3 and FT4 are nearly infinite. The Supplemental Declaration of W. Jean Dodds in Support of Patentability ("Supplemental Dodds Declaration"), submitted herewith, supports this.

The prior art did not provide any suggestion or motivation for one of ordinary skill in the art to contemplate an amount of the ranges for different optimal conditions as set out in the independent claims. Further, the prior art did not specifically contemplate an amount for adult optimal levels the criteria of FT3 is less than 8 pg/mL and FT4 is less than 3 ng/dL.

There is a lack of any credible teachings in the applied prior art itself which would appear to have fairly suggested the claimed subject matter as a whole to a person of ordinary skill in the art, or any viable line of reasoning as to why such artisan would have otherwise found the claimed subject matter to have been obvious in light of the teachings of the art. The prior art relied upon by the Examiner does not even recognize the problem addressed by the inventor of the present application, let alone suggest any of the claimed range limitations.

The present invention is clearly non-obvious, and not the work of mere routine experiment. Here, the Examiner cannot meet the additional KSR threshold tests, since the currently applied references do not teach the invention as claimed.

As Dodds points out in her Supplemental Declaration, no where does any prior art teach, disclose or suggest establishing for thyroid disease analysis in four categories. More specifically

there is no teaching, disclosure or suggestion of the optimal levels in each of four categories, namely the adequate optimal levels, the therapeutic response optimal levels, the minimal expectation optimal levels; or the optimal levels for autoimmune thyroiditis. There is no teaching disclosure or suggestion for establishing for thyroid disease analysis optimal levels, the levels being defined by a range different to a laboratory reference range as presented in the laboratory report, there being at least one category of the adequate optimal levels, therapeutic response optimal levels, the minimal expectations optimal levels; or the optimal levels for confirming autoimmune thyroiditis.

As such there no teaching, disclosure or suggestion of at least one category of the optimal adequate levels, optimal therapeutic response levels, the optimal minimal expectation levels; or the levels for autoimmune thyroiditis; assessing thyroid function as part of the preliminary analysis by determining the correct category, and an analysis based on the laboratory report as applied in the correct category to thereby obtain a supplemental report.

More so, none of these references remotely teach or suggest or disclose the adult optimal levels the criteria of FT3 is less than 8 pg/mL and FT4 is less than 3 ng/dL.

Thus, as submitted the current references are deficient in meeting the KSR standards and even more so now they are even further deficient. in teaching, suggestion, or motivation to combine them and thereby attain the invention as claimed.

In the context of the relevant art, namely thyroid diagnosis, there are not a small number of limited options which could have been chosen or selected by a skilled artisan. Indeed, there were several unpredictable alternatives to determine the exact route for a successful thyroid analysis. It would only be with hindsight, which is not the standard for obviousness, to discount the number and complexity of the alternatives.

At the time of the invention, it was the inventor's insights and willingness to confront and overcome the obstacles which led to the invention as claimed.

Applicant, in the present application, submits that Examiner has failed to satisfy the burden of establishing that such a problem exists. The Applicant went against conventional wisdom and provided a thyroid diagnosis protocol which is inventive in several different ways as defined in the different claims 1, 10 and 25:

The dependent claims recite specific ranges. The prior art is silent as to any related ranges. The Applicant respectfully points out to the Examiner that the claimed limitations are not simply unimportant modifications without criticality.

The Applicant submits that a prima facie case of obviousness has not been established. The Applicant submits that the prior art applied by the Examiner does not show the general conditions from which the optimal or workable ranges could be determined.

Supplementary Declaration of Dodds In Support of Patentability

Secondary characteristics can support the flexible TSM test which remains the primary guarantor against a non-statutory hindsight analysis. To support such findings, it is permissible to look at unexpected results, commercial success and copying as evidence of non-obviousness. As stated above, this evidence is not just a cumulative or confirmatory part of the obviousness calculus, but constitutes independent evidence of non-obviousness.

No one before the Applicant remotely achieved these results. The results were unexpected because the set of variables in the combination that were sought was impossible to realize prior to the Applicant's discovery. Surprisingly the Applicant was able to achieve an optimal range. The results are more than a mere difference in properties. The unexpected result is that the new properties differ so as to have been really unexpected.

Additionally, the Applicant submits that the experimental data comparing the closest prior art systems of the different Dodds systems, namely is a system without selectable icons, and indeed the ones illustrated in the Figures of Dodds (WO/2001/028415). As has been stated above this is not remotely selectable icons of the present kind as claimed in the application.

Filteau (US 2002/0188896) is not related to animal conditions and has nothing to do with thyroid disease. Moreover Filteau does not deal with reporting the analysis through a network to the clinical pathologist wherein the clinical pathologist has the patient record containing the data relating to the physical characteristics and family and breed history, and the clinical pathologist thereby makes a preliminary diagnosis of the animal health, and thereafter uses the icons.

No where does any prior art teach, disclose or suggest establishing for thyroid disease analysis at least one category of the optimal adequate levels, optimal therapeutic response levels, the optimal minimal expectation levels; or the levels for autoimmune thyroiditis; assessing thyroid function as part of the preliminary analysis by determining the correct category, and an analysis based on the laboratory report as applied in the correct category to thereby obtain a supplemental report as claimed in claims 1, 10 and 25.

No where does any prior art teach, disclose or suggest establishing for thyroid disease analysis optimal levels, the levels being defined by a range different to a laboratory reference range as presented in the laboratory report, there being at least one category of the adequate optimal levels, therapeutic response optimal levels, the minimal expectations optimal levels; or the optimal levels for confirming autoimmune thyroiditis.

Furthermore, no where does any prior art teach, disclose or suggest applying for the assessment of thyroid function for adult optimal levels the criteria of FT3 is less than 8 pg/mL and FT4 is less than 3 ng/dL as claimed in claims 46-48.

Furthermore, no where does any prior art teach, disclose or suggest establishing for thyroid disease analysis more than one category of the optimal adequate levels, optimal therapeutic response levels, the optimal minimal expectation levels; or the levels for autoimmune thyroiditis as set out in new dependent claim 49.

Commercial Success Provides Secondary Objective Evidence to Support Patentability

The Supplemental Dodds Declaration also supports that Hemopet, a non profit company, and the Assignee of the application has achieved significant commercial success with the testing procedures of the present claims, and the nexus between that success and the invented features.

Hemopet has performed since at least about 2005 about $1,000,000 per annum worth of tests with the invention. This figure has continues to grow at about 10 percent per annum. Competitor testing does not provide the reporting enhancements, and the diagnosis using the optimal range, and are cheaper in the market place. There has been no advertising of the testing, and as such this commercial success did not come through extensive advertising of the testing. Despite this the invention is commercial successful based on the very fact of the invention as defined in the claims as now submitted has earned an invaluable reputation for creating a testing protocol and reporting system that sets the industry standards for accuracy, quality and value. This testing is a worldwide success and continues to be sought from Hemopet from several countries of the world. The international commercial success is also probative of patentability.

Thus as indicated there is not even the remotest disclosure or suggestion of an icon or a GUI representative of the textual content to be added to the supplementary report. Nor is there any teaching of optimal ranges.

The Supplemental Dodds Declaration, an expert in the field of veterinary diagnostics and reporting, is included in support of the inventive aspects of the present invention, namely establishing for thyroid disease analysis at least one category of the optimal adequate levels, optimal therapeutic response levels, the optimal minimal expectation levels; or the levels for autoimmune thyroiditis; and assessing thyroid function as part of the preliminary analysis by determining the correct category, and an analysis based on the laboratory report as applied in the correct category to thereby obtain a supplemental report. The declaration also supports the criticality of the claimed range for diagnosing thyroid disease. The commercial success of the technology validates the unobviousness of the invention as now claimed

The invention provides an important advance in the field of blood testing for thyroid disease in animals and the overall manner of providing supplemental and enhanced reporting, and thyroid diagnosis.

It is respectfully submitted that all of the Examiner's objections have been successfully traversed and that the application is now in order for allowance. Accordingly, reconsideration of the application and allowance thereof is courteously solicited.

The Director is authorized to charge any additional fee(s) or any underpayment of fee(s), or to credit any overpayments to **Deposit Account Number 50-2638**. Please ensure that Attorney Docket Number 058034-011800 is referred to when charging any payments or credits for this case.

Respectfully submitted,

Date: August 11, 2008

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